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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/010,667	12/06/2001	Daniel E. Afar	511582001601	1346

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EXAMINER	
NICKOL, GARY B	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 01/08/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/010,667	AFAR ET AL.	
	Examiner	Art Unit	
	Gary B. Nickol Ph.D.	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 October 2003*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *40-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *40-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *1/23/2003* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

Response to Amendment

Paper No. 12_30_03

The Amendment filed 10-20-03 in response to the Office Action of April 15, 2003 is acknowledged and has been entered.

Claims 40-47 are pending and are currently under consideration.

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office Action.

Information Disclosure Statement

Reference JP11164691-A was considered in so far as applicants argue (Remarks, 10/20/03, page 6) there was a 79% alignment over 499 nucleotides with a nucleotide sequence set forth in said reference on pages 36-37 with nucleotide 66-1085 of SEQ. ID. No.: 1. (signed IDS attached with this Action).

New Rejection:

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it

pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 40-47 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The claims are drawn to various discrete peptides derived from the larger STEAP-1 (SEQ ID NO:2) polypeptide. However, the specification fails to teach or provide sufficient guidance to one of skill in the art how to *use* the claimed peptides with any predictability. For example, the specification teaches (page 19, line 20+) that polypeptides comprising amino acid sequences which are unique to a particular STEAP protein (relative to other STEAP proteins) may be used to generate antibodies which will specifically react with that particular STEAP protein. Indeed, the specification proposes (page 27, lines 28+) that cell surface STEAP-1 protein is expressed at very high levels in several human cancers, particularly prostate, bladder, colon and ovarian cancers, and Ewing sarcoma wherein radiolabeled antibodies specifically reactive with extracellular epitopes of STEAP-I may be particularly useful in *in vivo* imaging of solid tumors of the foregoing cancers. The specification further teaches that such labeled anti-STEAP-1 antibodies may provide very high-level sensitivities for the detection of metastasis of these cancers. However, Table 1 on page 43 clearly indicates that anti-STEAP1 polyclonal antibodies have a strong staining intensity for normal prostate tissue, BPH, and prostate cancer. Thus, since the sensitivity of the detection of STEAP-1 is similar for both prostate cancer and *normal* prostate tissue, it would be unpredictable that anti-STEAP1 antibodies would predictably differentiate between normal versus the cancerous state. Furthermore, the specification teaches

(page 43, line 15) that cell surface expression of STEAP-1 in *normal* tissues appears to be restricted to prostate and bladder. Thus, since the disclosure does not appear to teach a discernible difference in the staining patterns of normal prostate and or normal bladder tissue versus anti-STEAP-1 staining in cancerous prostate and or cancerous bladder staining, it remains unclear how anti-STEAP-1 antibodies could be used in a predictable manner to positively image solid tumors versus their normal counterparts.

If a molecule such as STEAP-1 is to be used as a surrogate for a diseased state, some disease state must be identified in some way with the molecule. There must be some expression pattern that would allow the claimed polypeptide to be used in a diagnostic manner. Many proteins, including STEAP-1, are expressed in normal tissues and diseased tissues. Therefore, one needs to know, e.g., that the claimed polypeptide is present only in cancer tissue to the exclusion of normal tissue. Thus, in the absence of any correlation between the claimed peptides with any known disease or disorder, any information obtained from various expression profiles in both normal and diseased tissue only serves as the basis for further research on the observation itself. Therefore, absent evidence of the **protein's** expression including the correlation to a diseased state, one of skill in the art would not be able to predictably use the peptides in any diagnostic setting without undue experimentation.

Lastly, it is recognized that there was NO detectable staining of STEAP-1 in normal colon and ovarian tissues (Table 1, page 43). In contrast, Figure 6 indicates the presence of STEAP-1 in colon and ovarian cell lines. However, it is well known in the art that cultured cells, over a period time, lose phenotypic characteristics associated with their normal counterpart cell type. Freshney (Culture of Animal Cells, A Manual of Basic Technique, Alan R. Liss, Inc., 1983,

New York, p4) teaches that it is recognized in the art that there are many differences between cultured cells and their counterparts *in vivo*. These differences stem from the dissociation of cells from a three-dimensional geometry and their propagation on a two-dimensional substrate. Hence, specific cell interactions *characteristic of the histology* of the tissue are lost. The culture environment lacks the input of the nervous and endocrine systems involved in homeostatic regulation *in vivo*. Without this control, cellular metabolism may be more constant *in vitro* but may not be truly representative of the tissue from which the cells were derived. This has often led to tissue culture being regarded in a rather skeptical light (p. 4, see Major Differences *In Vitro*). Further, although drawn specifically to cancer cells, Dermer (Bio/Technology, 1994, 12:320) teaches that, "petri dish cancer" is a poor representation of malignancy, with characteristics profoundly different from the human disease. Further, Dermer teaches that when a normal or malignant body cell adapts to immortal life in culture, it takes an evolutionary type step that enables the new line to thrive in its artificial environment. This step transforms a cell from one that is stable and differentiated to one that is not. Yet normal or malignant cells *in vivo* are not like that. The reference states that evidence of the contradictions between life on the bottom of a lab dish and in the body has been in the scientific literature for more than 30 years. Clearly it is well known in the art that cells in culture exhibit characteristics different from those *in vivo* and cannot duplicate the complex conditions of the *in vivo* environment involved in host-tumor and cell-cell interactions. Hence, in the absence of a correlation of STEAP-1 staining in either cancerous colon or ovarian tissue specimens versus their normal tissue counterparts, the evidence of record suggests a high degree of unpredictability that STEAP-1 would be expressed

differentially between these types of cancers. Thus, it would require undue experimentation to practice the method as claimed.

All other rejections and or objections are withdrawn in view of applicant's amendments and arguments there to.

No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Gary B. Nickol Ph.D. whose telephone number is 703-305-7143. The examiner can normally be reached on M-F, 8:30-5:00 P.M..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 703-308-3995. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Gary B. Nickol, Ph.D.
Examiner
Art Unit 1642

GBN
December 30, 2003

Gary B Nickol